STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 129546

TO: Leon Y Lum
Location: REM/3D78/3C70
Art Unit: 1641
Sunday, August 15, 2004
Case Serial Number: 10/044708

From: Paul Schulwitz
Location: Biotech-Chem Library
REM-1A65
Phone: (571)272-2527

paul.schulwitz@uspto.gov

Search Notes

Examiner Lum,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
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(571)272-2527

Access DB# 104546

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Lan Lum Examiner #: 80278 Date: 8/9/04
Art Unit: 1641 Phone Number ~~30~~ 2-2878 Serial Number: 10/044708
Mail Box and Bldg/Room Location: Remsen Bldg. Results Format Preferred (circle): PAPER DISK E-MAIL
Mailbox: 3C70
Room: 3D78

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantification using matrix-assisted laser desorption ionization mass spectrometry

Inventors (please provide full names): Yong-dong Qin, ~~Jack Wong~~, Rodney M. Hewick, Jack H. Wang

Earliest Priority Filing Date: 10/23/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the structures of claim 9 (see attached) and the following search terms:

D = Deuterium

Matrix Assisted Laser Desorption / Ionization (MALDI)

Mass Spectrometry (MS)

MALDI-MS

Isotope Coded Affinity Tags (ICAT)

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	730.42
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	2	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed:	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time:	Other		Other (specify)	

WHAT IS CLAIMED IS:

1. A method for enhancing identification and relative quantitation of proteins and peptides using mass spectrometry (MS), said method comprising the steps of:

(a) reducing the disulfide bonds of a first sample from a biological mixture containing proteins and peptides;

(b) labeling proteins and peptides in the first sample with a reagent which comprises a thiol-specific reactive group attached to a guanadino group via a linker which can be differentially labeled;

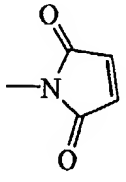
(c) separating the proteins and peptides from the sample;

(d) digesting the proteins to provide a mixture containing digestion peptides and peptides from the first sample; and

(e) subjecting the peptides of (d) to quantitative MS analysis and protein identification.

2. The method according to claim 1, wherein the peptides of (d) are subjected to matrix-assisted laser desorption/ionization (MALDI) - MS.

3. The method according to claim 1, wherein the reagent comprises a thiol-specific reactive group is selected from the group consisting of α-haloacetyl (-X-CH_2CO-, X = I, Br, or Cl) or a maleimide group having a structure selected from the group consisting of:



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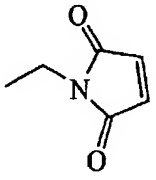


12,29 - 12,54

(29)

4. The method according to claim 1, wherein the linker comprises an alkyl chain having three to eight carbon atoms, optionally substituted with one or more amido groups, carboxy groups, or amino groups.

5. The method according to claim 1, wherein the proteins and peptides are further subjected to peptide mass mapping, said method further comprising the steps of:

labeling proteins and peptides in a second sample with said reagent having heavy stable isotopes; and

mixing the first and second samples prior to the separation step,

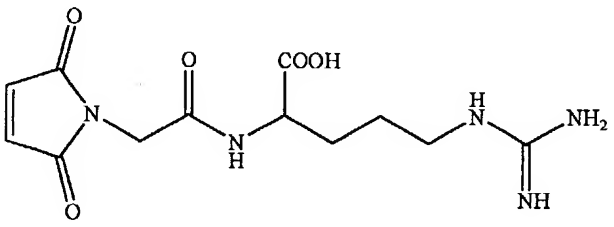
wherein the reagent in the labeling step contains light stable isotopes.

6. The method according to claim 1, wherein the linker in the reagent of step (b) contains a substitution of four to twelve atoms with a stable isotope.

7. The method according to claim 6, wherein the linker contains seven stable isotopes.

8. The method according to claim 6, wherein the hydrogen atoms are substituted with deuterium.

9. The method according to claim 5, wherein the reagent is selected from the group consisting of:



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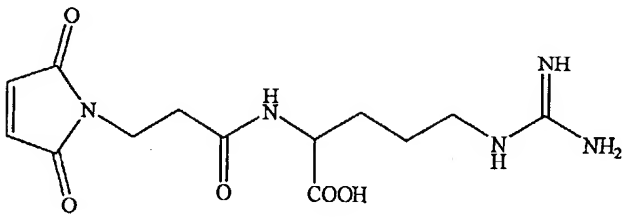
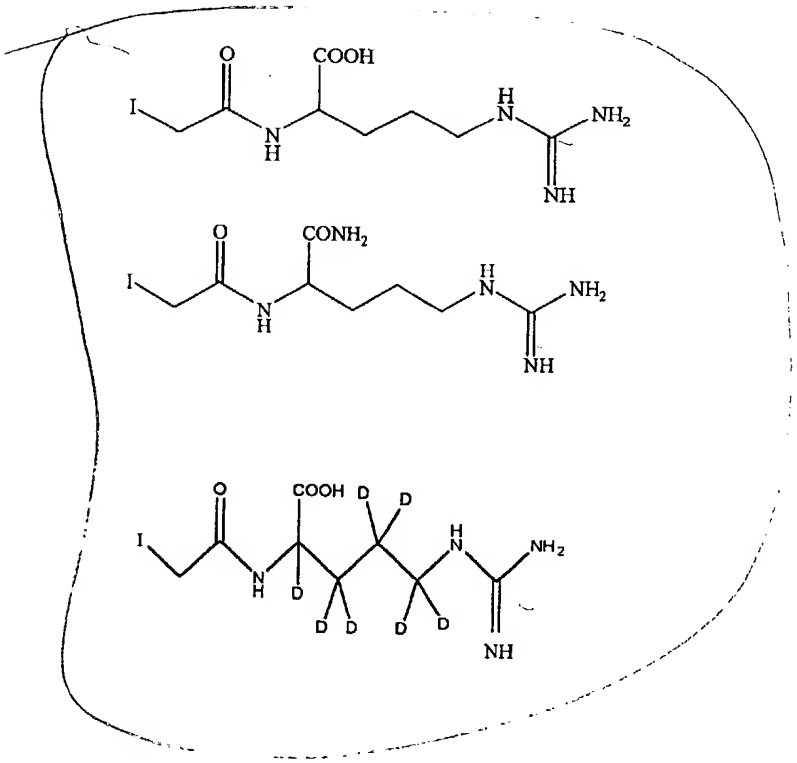




and

10. The method according to claim 5, wherein the separation step is performed using one dimensional or two dimensional polyacrylamide gel electrophoresis (1D or 2D-PAGE), or liquid chromatography.

11. The method according to claim 1, wherein the digestion step is performed in-gel or in solution.

12. A method for preparing peptides for MALDI-MS and subsequent data analysis, said method comprising the steps of:

(a) reducing the disulfide bonds of proteins from biological samples;

(b) labeling proteins in one sample with a reagent which comprises a thiol-specific reactive group attached to a guanidino group via a linker which is differentially labeled with light stable isotopes;

(c) labeling proteins in a second sample with a reagent having heavy stable isotopes;

(d) mixing the first and second labeled samples;

(e) separating the proteins from the mixture;

(f) digesting the proteins, thereby providing peptides ready for MALDI-MS analysis and protein identification.

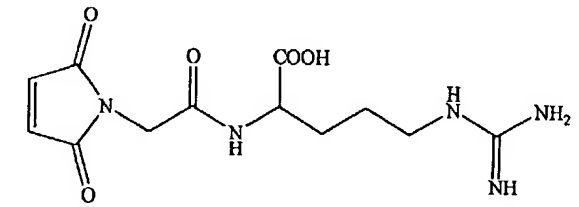
13. The method according to claim 11, wherein the digestion step is performed using trypsin.

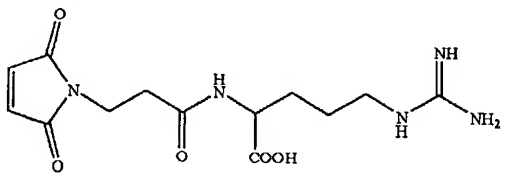
14. A compound useful in quantitative analysis of protein mixtures, said compound comprising a thiol-specific reactive group attached to a guanidino group via a linker which can be differentially labeled with stable isotopes.

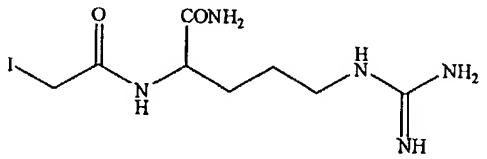
15. The compound according to claim 14, wherein the linker contains four to twelve stable isotopes.

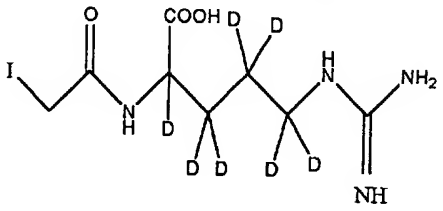
16. The compound according to claim 14, wherein the linker contains a substitution of at least six hydrogen atoms with deuterium.

17. The compound according to claim 14, selected from the group consisting of:









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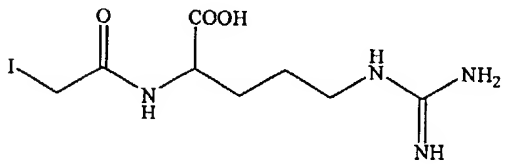

18. A reagent kit for the analysis of proteins by mass spectrometric analysis that comprises a compound of claim 14 or claim 17.

19. The reagent kit according to claim 18, comprising a set of substantially identical differentially labeled alkylating reagents.

20. The reagent kit according to claim 18, further comprising one or more proteolytic enzymes for use in digestion of proteins modified by said compounds.

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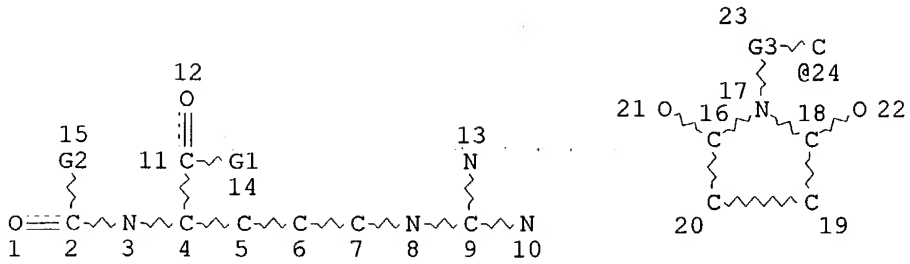
L13 STR



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25 @26

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VAR G2=24/26
REP G3=(0-4) C
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DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L15 2 SEA FILE=REGISTRY SSS FUL L13
L16 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

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L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:78612 HCAPLUS
DOCUMENT NUMBER: 68:78612
TITLE: Potential antiviral agents. Carbobenzoxy di- and tripeptides active against measles and herpes viruses
AUTHOR(S): Nicolaides, Ernest D.; De Wald, Horace A.; Westland, Roger D.; Lipnik, Marilyn; Posler, Jeanette
CORPORATE SOURCE: Parke, Davis and Co., Ann Arbor, MI, USA

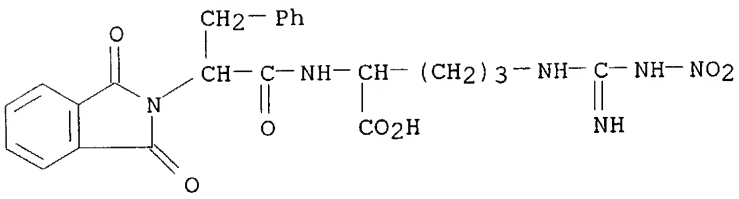
SOURCE: Journal of Medicinal Chemistry (1967), 11(1), 74-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A large number of carbobenzoxy dipeptides, several tripeptides, and a number of alkyl, cycloalkyl, aryl, and heterocyclic amide derivs. of carbobenzoxy-L-and D-phenylalanine were synthesized. Many of the peptides were active against measles and herpes viruses.

IT **17461-57-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 17461-57-3 HCAPLUS

CN Ornithine, N5-(nitroamidino)-N2-(L-α-phthalimidohydrocinnamoyl)-, L- (8CI) (CA INDEX NAME)



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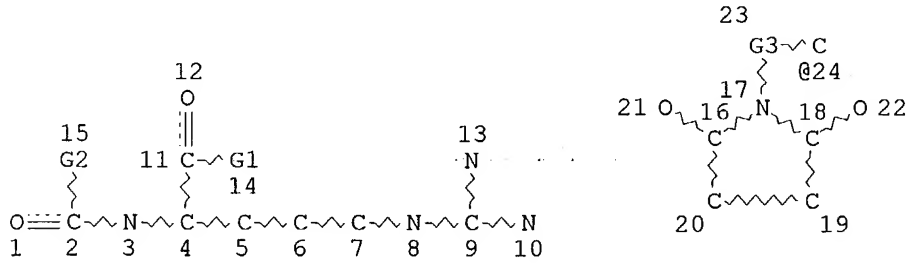

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VAR G1=OH/NH2
VAR G2=24/26
REP G3=(0-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L19 2 SEA FILE=MARPAT SSS FUL L13
L20 1 SEA FILE=MARPAT ABB=ON PLU=ON L19/COM

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L20 ANSWER 1 OF 1 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:34581 MARPAT
TITLE: Preparation of acetylene derivatives for inhibition of matrix metalloproteases
INVENTOR(S): Dixon, Brian R.; Chen, Jinshan
PATENT ASSIGNEE(S): Bayer Corporation, USA; Dixon, Brian R.; Chen, Jinshan
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743245	A1	19971120	WO 1997-US7921	19970512
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ZA 9704031	A	19980219	ZA 1997-4031	19970509
HR 970245	B1	20020630	HR 1997-970245	19970509
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AU 710759	B2	19990930		
EP 912496	A1	19990506	EP 1997-923622	19970512
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BR 9709077	A	19990803	BR 1997-9077	19970512
CN 1225623	A	19990811	CN 1997-196456	19970512
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JP 3090957	B2	20000925		
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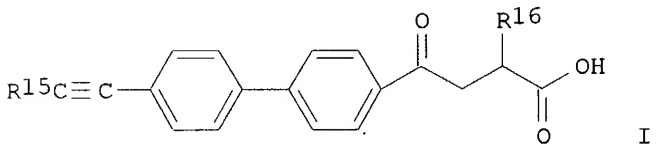

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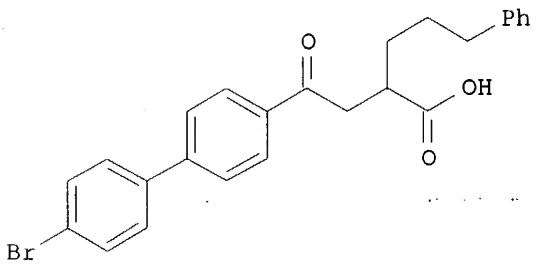
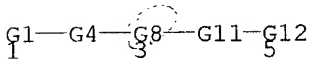


II

AB The title compds. [I; R15 = HOCH2, MeOCH2, CH3CO2CH2, EtOCO2CH2, HO(CH2)2, CH3CO2(CH2)2, HO2C(CH2)2, OHC(CH2)3, HO(CH2)4, Ph, etc.; R16 = Ph(CH2)3, phthalimidoethyl] are prepared I are useful for inhibiting matrix

metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis, bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempero mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plate rupture. Thus, compound (II) was reacted with HOCH2C.tplbond.CH in the presence of Et2NH, CuI, and trans-dichlorobis(triphenylphosphine)palladate to give I [R15 = HOCH2, R16 = Ph(CH2)3], which showed IC50 of 21 μM against MMP-3.

MSTR 2



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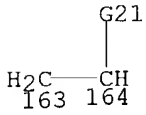

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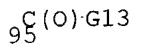

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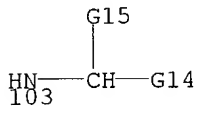

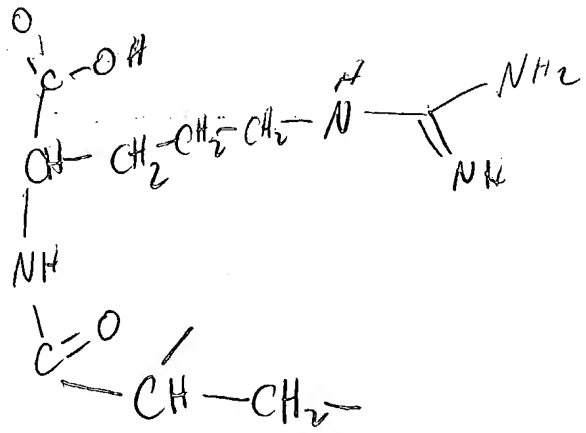

G14 = CO2H
G15 = CH2CH2CH2NHC(NH)NH2
G22 = (1-5) CH2
G24 = phthalimido
DER: and pharmaceutically acceptable salts
MPL: disclosure
NTE: Ak in G11 may contain cyclic groups

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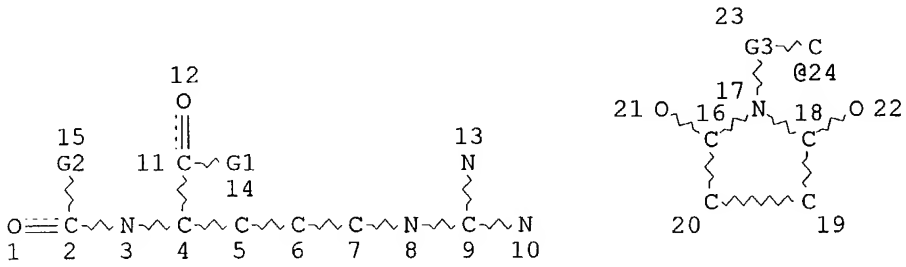
L13 STR



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VAR G2=24/26
REP G3=(0-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L17 0 SEA FILE=BEILSTEIN SSS FUL L13